

PHILIP MORRIS INCORPORATED
LAW DEPARTMENT MEMORANDUM
RICHMOND, VIRGINIA

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CPF

TO: T. Osdene DATE: April 11, 1983
FROM: G. Inskeep
SUBJECT: OPTICALLY ACTIVE NICOTINE ANALOGS AND PROCESS FOR
THEIR PREPARATION/USSN 377,990/PM 893 DIV I

For your information, we attach a copy of the Official Action recently received in this case.

If you have any comments to offer before we begin preparation of a response, please let me know. We prefer not to have you or the inventor(s) write anything at this stage about the Action or the invention, or go to any trouble interpreting or analyzing the Action. At the appropriate time, we will arrange to get from the inventor(s) anything needed to help us in preparing a response.

On the other hand, if it should appear to you that the case might not be worth pursuing, please call to give me your views on that aspect.

bjm:

cc: W. Edwards, III
E. Sanders
S. Hutcheson

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Art Unit 121

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26 and 27 are rejected under 35 U.S.C. 103 as being unpatentable over Noller, Roberts et al. Buehler et al. and March.

The Noller text teaches in Page 613 that pyrrolecarboxylic acids lose carbon dioxide upon heating a behavior characteristic of phenolcarboxylic acids. The Roberts et al. text teaches in Page 1002 that furoic acid, pyrrolecarboxylic acid and resorcinol -2-carboxylic acid which also decarboxylates on heating. The is much more satisfactory for aromatic and heterocarboxylic acids compared to the aliphatic counterparts and said decarboxylation can

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be conducted in alkaline or acidic conditions. In both pages the esters are taught to undergo decarboxylation analogously to the acids from which they are derived. Note teaching in page 53 that Ester (or acid) groups attached to aromatic rings mainly (mainly phenols), susceptible to electrophilic attack, are decarboxylated readily with acid. The March text teaches in Page 514 that decarboxylation of aromatic acids can be carried out by a variety of methods including heating said acid in presence of a strong acid such as sulfuric. Also, a salt of a carboxylic acid may be heated as the acid itself to accomplish decarboxylation. Note that the teaching in page 514 includes the electron donating groups in ortho or para positions and by steric effect of groups in ortho positions. The combination of the 4 references is believed to render obvious the claimed decarboxylation reaction of a pyrrolidine carboxylic acid under acidic conditions, no other conditions are specified.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or

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described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33, 34 and 39 are rejected under 35 U.S.C. 102b as being anticipated by Cushman et al..

Specifically, The Cushman et al. article in J. of Org. Chem., Vol. 37, No. 8, (1972) teaches in Pages 1268-71 the compounds 2-pyrrolidinones wherein the term R in the depicted formula in Page 1269 represents methyl; the term "Ar" represents 3-pyridyl, the term R_2 represents hydrogen; the term R_1 represents $-COOCH_3$; the concept of absolute stereochimistry with 2'S, 3'S and 3 R enantiomer are also taught in Page 1269 supra. Said compounds clearly read on the instant claims.

Claims 33-39 are rejected under 35 U.S.C. 103 as being unpatentable over Cushman et al. and March.

The Cushman et al. reference was shown above to disclose a few compounds that clearly read on the instant claims; methods for their preparation are also shown. Other than clearly reading on a few of these claims said reference compound are homologues

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of the remaining claims raising a presumption of obviousness. The March text teaches in pages 108-111 a complete teaching on resolution and optical purity. The combination of references is believed to be suggestive of the claimed compounds within purview of 35 U.S.C. 103.

Claims 54 and 55 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 54 and 55 of applicant's of applicant's copending application S.N. 377,989. This is a double patenting rejection.

Specifically, the claims of both copending applications are identical. See *In re Ochert*, 114 U.S.P.Q. 330.

Claim 54 is rejected under 35 U.S.C. 102a as being anticipated by Morrin et al..

Specifically, the Morrin et al. article abstracted by Chem. Abstracts, Vol. 93, No. 13, item No. 132,669 discloses the compound of formula I wherein (R and R¹) represents oxo; the terms R² and R³ represent methyl in the (S) or sinister optically active form which clearly reads on the instant claim.

Claim 55 is rejected under 35 U.S.C. 103 as being unpatentable over Morrin et al..

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The disclosure of Morrin has been discussed above with respect to the (S) or sinister absolute configuration which is the counter part of the (R) or rectus configuration of claim 55. Optical isomers are not patentable over each other absent a showing of unexpected results. *In re Adamson*, 125 U.S.P.Q. 233.

Applicant is required to make a prior art statement in compliance with 37 CFR 1.97-1.99.

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ALAN L. ROTMAN
EXAMINER
GROUP ART UNIT 121

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T. S. OSDENE

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